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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CHERNYSHEV, OLGA N	
ART UNIT	**PAPER NUMBER**
1646	8

DATE MAILED: 09/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/099,880	Applicant(s) WEKSLER ET AL.
	Examin r Olga N. Chernyshev	Art Unit 1646

-- The MAILING DATE of this communication appears on th cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *19-26 and 28-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1-18 and 27, in Paper No. 6 is acknowledged.

Claims 19-26 and 28-30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 6.

Claims 1-18 and 27 are under examination in the instant office action.

Information Disclosure Statement

2. The information disclosure statement filed 6/28/2, Paper No. 4, fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. Specifically, the references 33-72 listed in IDS of Paper No. 4 are not present among the papers provided. The IDS has been placed in the application file, but the information referred to publications 33-72 therein has not been considered.

Specification

3. The abstract of the disclosure is objected to because it does not comply with 37 C.F.R. § 1.72 with regard to format.

37 C.F.R. § 1.72 states "The abstract in an application filed under 35 U.S.C. 111 may not exceed 150 words in length". See also MPEP § 608.01(b), which states, "The abstract should be

in narrative form and generally limited to a single paragraph within the range of 50 to 150 words", emphasis added. Correction is required.

Claim Objections

4. Claim 7 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 7 appears to be directed to the same invention as claim 1 from which it depends because the conclusion of claim 1 recites indication of the presence of a neurodegenerative disease or disorder, which is ordinary considered to be "diagnosing" disease or disorder. See also reasons of record in sections 9 and 12 below in the instant office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-18 and 27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for assessing risk of a subject of having an Alzheimer's disease by comparing a level of anti-Aβ_{42} antibody in a serum sample from a subject to a normal level, which is determined from an average of the level of anti-Aβ_{42} antibody in a serum sample from a population of age-matched normal subjects who do not show any

symptoms of Alzheimer's disease, wherein a lower level indicates the risk of having an Alzheimer's disease, does not reasonably provide enablement for a method for assessing risk of a neurological disease by comparing a level of anti-Aβ_{42} antibody in a biological sample, wherein a lower level indicates the presence of a neurological disease, including Alzheimer's disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claims 1-9 and 17 are directed to a method for assessing risk of a neurological disease by comparing a level of anti-Aβ_{42} antibody in a biological sample, wherein a lower level indicates the presence of a neurological disease. Claims 10-16, 18 and 27 are directed to a method for assessing risk of Alzheimer's disease by comparing a level of anti-Aβ_{42} antibody in a biological sample, wherein a lower level indicates the presence of Alzheimer's disease. However, the instant specification fails to provide enough guidance for one skilled in the art on how to practice the instant methods, thereby requiring undue experimentation to discover how to practice Applicant's invention commensurate in scope with the instant claims.

The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. *In re Wands*, 8 USPQ2d, 1400 (CAFC 1988).

The nature of the invention is the demonstration that serum levels of anti-Aβ_{42} antibodies in samples obtained from patients with probable Alzheimer's disease (AD) are significantly

lower than serum levels of anti-Aβ_{42} antibodies of elderly adults without AD, see pages 18-21 of the instant specification. This finding appears to be novel because at the time of the invention there is no disclosure in the art regarding the difference of anti-Aβ_{42} antibody levels in any biological samples between AD patients and normal control individuals.

However, the instant claims are not limited to a method for assessing risk of a subject of having an Alzheimer's disease by comparing a level of anti-Aβ_{42} antibody in a serum sample from a subject to a normal level, wherein a lower level indicates the risk of having an Alzheimer's disease. Claims 1-9 and 17 are directed to a method for assessing risk of a neurological disease by comparing a level of anti-Aβ_{42} antibody in a biological sample, wherein a lower level indicates the presence of a neurological disease, emphasis added. Note that with regard to claim breadth, the standard under 35 U.S.C. §112, first paragraph, entails the determination of what the claims recite and what the claims mean as a whole. In addition, when analyzing the enablement scope of the claims, the teachings of the specification are to be taken into account because the claims are to be given their broadest reasonable interpretation that is consistent with the specification. As such, the broadest reasonable interpretation of the claimed method is that by comparing levels of anti-Aβ_{42} antibody in a subject to a normal level, the presence of a neurodegenerative disease or disorder can be determined. One skilled in the art readily recognizes that term "neurodegenerative disease or disorder" is very broad and includes, by different art recognized classifications, plurality of pathological conditions of different etiology, including Parkinson's disease, Huntington's disease, prion diseases, different forms of dementia etc. (see, for example reference by Hardy et al., 1998, Science, Vol.282, pp.1075-1079). Note that most of neurodegenerative diseases are not associated with amyloid-like

pathology (see Table 1 on page 1077, for example). The instant specification fails to provide any evidence or sound scientific reasoning that would support a conclusion that limited data obtained from patients diagnosed with probable AD could be successfully extrapolated to diagnose any neurodegenerative disease or disorder. Furthermore, the instant specification provides no evidential support for concluding that any biological sample contains anti-$A\beta_{42}$ antibodies in measurable amounts, such samples would include bone tissue samples, saliva or urine samples. Also, the working examples regarding anti-$A\beta_{42}$ antibody levels in neurodegenerative diseases are limited to data obtained from eight patients with unidentified neurological diseases, which appear to be inconclusive (see page 21 and Table 3 on pages 22-23 of the instant specification).

Thus, Applicant's invention is predicated on the finding that serum levels of anti-$A\beta_{42}$ antibodies in samples obtained from patients with probable Alzheimer's disease are significantly lower than serum levels of anti-$A\beta_{42}$ antibodies of elderly adults without AD. Applicant further extrapolates these results into a method for assessing risk of any neurodegenerative disease or disorder by comparing the levels of anti-$A\beta_{42}$ antibodies. Accordingly, it would appear that Applicant provides a single finding (the finding), and then presents an invitation to experiment to determine if or which other neurodegenerative diseases or disorders also are characterized by different levels of anti-$A\beta_{42}$ antibodies, and then to assay to establish values of normal levels of anti-$A\beta_{42}$ antibodies as well as specificity of a biological sample.

Further, claims 10-16, 18 and 27 are directed to a method for assessing risk of Alzheimer's disease by comparing a level of anti-$A\beta_{42}$ antibody in a biological sample, wherein a lower level indicates the presence of Alzheimer's disease. It is well recognized in the art that the definitive diagnosis of Alzheimer's disease could be made only during postmortem

examination of brain tissue (see Motter et al. 1995, Annals of Neurology, Vol.38, No.4, pp.643-648; Clark et al., 1993, Arch. Neurology, Vol.50, pp.1164-1172, for example). It is also stated in the instant specification that "[p]atinets with AD [...] met the NINCDS-ADRDA criteria for Probable AD", emphasis added (page 18 lines 9-10). Therefore, based on the knowledge in the art and the information provided in the instant specification, one would reasonably conclude that the instant specification provides adequate support only for a method of assessing a risk of one having an AD, and not for a method for definitive diagnosis of AD. Moreover, the instant specification fails to provide any evidence or sound scientific reasoning to support a conclusion that any biological sample would be suitable for anti-Aβ_{42} antibody levels measurements (see reasons of record earlier in this section of the instant office action). There is also no indication submitted that a normal level could be determined from an average of the level of anti-Aβ_{42} antibody in a biological sample from a population of all subjects, as recited in claim 13.

A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of *Genentec, Inc, v. Novo Nordisk*, 42 USPQ 2d 100,(CAFC 1997), the court held that:

"[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure". The court further stated that "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[i]t is the specification, not the knowledge of one

skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

The instant specification is not enabling because one can not following the guidance presented therein and practice the full scope of the claimed methods without first making a substantial inventive contribution to discover how to use Applicants' invention as currently claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-18 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claims 1 and 10 are vague and indefinite for recitation "a normal level". Because the definition of "normal level" provided in the instant specification on page 3, lines 12-18, includes determination from an average of the level of anti-amyloid peptide antibody in the biological samples from a population of age-matched normal subjects, or all subjects or from a single normal sample, the metes and bounds of recitation "normal level" cannot be determined from the claims. See also reasoning regarding normal level of anti-amyloid antibodies in any biological sample in section 5 earlier in the instant office action. Applicant is advised that including limitations, which would clearly define how to establish "a normal level", or including values of the normal level, as presented in the instant specification on pages 19-20, for example, would obviate this ground of rejection.

8. Claims 1, 10 and 16 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the steps of determination of levels of anti-Aβ_{42} antibody.

9. Claims 1, 10 and 16 are further indefinite because it appears that the preamble of the claims ("assessing risk of") is inconsistent and in conflict with the conclusion ("indicates the presence of"). Clarification is required.

10. Claims 3 and 4 recite the limitation " anti-Aβ_{42} peptide antibody " and claim 5 recites the limitation " anti-Aβ_{42} antibody " in claim 1. Claims 12, 13 and 14 recite the limitation " anti-amyloid peptide antibody " in claim 10. There is insufficient antecedent basis for these limitations in the claims. Applicant is advised to use consistent terminology throughout the claims to obviate this ground of rejection.

11. Claims 5 and 14 recite the limitation "determining" in claims 1 and 10, respectively. There is insufficient antecedent basis for this limitation in the claim.

12. Claim 7 is vague and ambiguous because it appears to be not further limiting in view of reasons of record in section 9 of the instant office action. Briefly, one would ordinary consider that indication of the presence of a disease equals to diagnosing a disease. Clarification is required.

13. Claims 9 and 18 are indefinite for recitation "in his or her seventh or eighth decade". Applicant is advised that recitation of "in his or her seventh or eighth decade of life", perhaps, would obviate this ground of rejection.

14. Claim 16 is vague and ambiguous for recitation "from a subject to a normal level". The claim appears to be confusing and difficult to understand. Applicant is advised to rewrite the claim to better articulate the claimed subject matter.

15. Claims 2, 6, 8, 11, 15, 17 and 27 are indefinite for being dependent from indefinite claims.

Double Patenting

16. Claim 17 objected to under 37 CFR 1.75 as being a substantial duplicate of claim 8. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Conclusion

17. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (703) 305-1003. The examiner can normally be reached on Monday to Friday 9 AM to 5 PM ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)0. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 872-9306. If this number is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (703) 308-7939. Official papers should NOT be faxed to (703) 308-7939.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Olga N. Chernyshev, Ph.D.